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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,829	03/29/2004	Alan D. King	04-100	9996

7590 03/06/2006

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EXAMINER	
FERNANDEZ, SUSAN EMILY	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,829	KING ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26,28-31,37,38,40,42,44,47-50 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,26,28-31,37,38,40,42,44,47-50 and 52* is/are rejected.

7)☒ Claim(s) *28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendments filed February 13, 2006, have been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

The finality of the previous office action has been withdrawn. Claims 25, 26, 28-31, 37, 38, 40, 42, 44, 47-50, and 52 are pending and examined on the merits.

Claim Objections

Claim 28 is objected to because of the following informalities: the claim recites "wherein said parallel rows of electrodes include needle electrodes" which is already required by the claim, since the electrode assembly of claim 26 is a plurality of needle electrodes. It is suggested that "and wherein said parallel rows of electrodes include needle electrodes" be deleted. Appropriate correction is required.

Claim Rejections - 35 USC § 102

Claim 42 is rejected under 35 U.S.C. 102(e) as being anticipated by Wang (US Pat. 6,514,762).

Wang discloses a device comprising two electrodes coated by nucleotides (column 2, lines 38-40) such as DNA and RNA (column 2, lines 65-67). The device allows for the delivery of nucleotides for "use in gene therapy for treatment or prevention of disease" (column 4, lines 16-19). Thus, Wang provides a method for DNA or RNA vaccine delivery, as a vaccine is used

for disease prevention. In particular, the nucleotides may be used for treatment of cancer (column 8, lines 5-7).

Note that the electrodes of the Wang device may be needle electrodes. See column 19, lines 33-45.

Applicant's arguments filed August 19, 2005, have been fully considered but they are not persuasive. While claims 25, 26, 28, 29, 31, 37, 38, 40, 44, 47-50, and 52 of the instant application have an effective filing date of January 28, 1999, claims 30 and 42 do not as they cannot claim the benefit of Provisional Application 60/117,755. The disclosure of the prior-filed application, 60/117,755, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for claims 30 and 42 of this application.

With respect to the argument that unlike Wang, the Applicant's claimed invention does not require time release of nucleotides and instead, the electrode delivers a pre-measured dose, it is respectfully pointed out that claim 42 and its parent claims 25 and 37 do not recite the requirement of the delivery of a pre-measured dose. Thus, a holding of anticipation is required.

Claim Rejections - 35 USC § 103

Claims 25, 26, 28, 29, 30, 31, 37, 49, 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidlich et al. (US 5,103,837) in view of Hofmann (U.S. 6,009,347).

Weidlich et al. teaches an implantable, stimulating electrode which is coated with a hydrophilic polymer which comprises an anti-inflammatory steroid (claim 1). The anti-inflammatory steroid diffuses after implantation into surrounding tissue (claim 1). Though not expressly stated, it is clear that when the electrode is implanted, the steroid is delivered into

biological cells in the tissues penetrated by the electrode by the electric field applied to the penetrated tissues. Thus, Weidlich et al. discloses limitations in instant claims 25, 29, 31, 37, and 52.

Additionally, Weidlich et al. discloses that the hydrophilic polymer can be Nafion which is gel-like (column 2, lines 30-37), and therefore teaches the limitation of instant claim 30. Furthermore, the reference discloses the limitations in instant claim 49 (column 4, lines 1-7).

Note further that instant claims 49 and 50 are product-by-process claims. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. "[T]he lack of physical description in a product-by-process claim makes

determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). Thus, Weidlich et al. may be applied to teach the limitations of claim 50 under examination.

Weidlich et al. differs from the claims in that electrodes are not expressly disclosed as being needle electrodes.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have used needle-like electrodes for preparing the Weidlich invention since needles are suitable means for injections in the body. Moreover, it would have permitted access to more deeply located cells in the body.

Additionally, Weidlich et al. does not expressly disclose an electrode assembly, or that the electrode assembly comprises of at least two parallel rows of electrodes.

Hofmann discusses electroporation for use in introducing foreign material into living cells (column 1, lines 9-14 and lines 34-40). Specifically, Hofmann discloses using needle electrodes (column 4, lines 33-35) and notes that "the applicant has found through experimentation that pulsing between multiple pairs of electrodes in a multiple electrode array,

preferably set up in rectangular or square patterns, provides improved results over that of pulsing between a pair of electrodes" (column 4, lines 49-53). The electroporation device may comprise of an array of needles as electrodes (column 4, lines 53-61).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have modified the Weidlich invention such that needle electrodes set up in electrode arrays of multiple rows of electrodes are used to create the stimulating electrodes of Weidlich et al. One of ordinary skill in the art would have been motivated to do this because electrode arrays result in improved drug delivery (column 4, lines 49-53). Furthermore, Hofmann indicates that needle-shaped electrodes allow for access to more deeply located cells (column 1, lines 44-45).

Applicant's arguments filed August 19, 2005 and February 13, 2006, have been fully considered but they are not persuasive. Applicants notes that Hofman teaches electrodes which do not have a coating having at least one static layer of releasable molecules to be delivered into biological cells in the penetrated tissues by an applied electric field. However, Hofmann is not applied alone, but in combination with another reference, which teaches this limitation, and the claimed invention becomes obvious when the references are considered together as a whole rather than each alone. The Hofmann reference is discussed in order to provide motivation for creating an electrode array of the Weidlich electrodes, and also to provide further motivation for using needle-shaped electrodes.

Claims 25, 26, 28, 29, 30, 31, 37, 38, 40, 42, 47, 49, 50, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidlich et al. and Hofmann as applied to claims 25,

26, 28, 29, 30, 31, 37, 49, 50, and 52 above, and further in view of Zewert et al. (U.S. 5,749,847) and/or Widera et al. (Journal of Immunology, 2000, 164: 4635-4640).

As discussed above, Weidlich et al. and Hofmann render claims 25, 26, 28, 29, 30, 31, 37, 49, 50, and 52 obvious. However, these references do not expressly disclose vaccines, including polynucleotide, DNA, and RNA vaccines, in the polymeric coating of the implantable, stimulating electrode taught by Weidlich et al.

Zewert et al. teaches the use of electroporation for the delivery of nucleotides into an organism (column 2, lines10-14). More specifically, a composition comprising the nucleotide(s) is applied to the skin, and the skin is subsequently electroporated. The composition applied to the epidermis for drug delivery may include a vaccine (column 4, lines 32-34), and appropriate nucleotides for delivery include polynucleotides, deoxyribonucleotides (column 3, lines 44-46), and ribonucleic acid (column 4, lines 44-46).

Widera et al. discloses DNA vaccine delivery facilitated by electroporation (abstract). Needle array electrodes were used for electroporation following the injection of DNA or a DNA vaccine (page 4636, first column, "DNA immunization and in vivo electroporation").

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have included polynucleotide, DNA, and RNA vaccines in the polymeric coating of the Weidlich electrode to be delivered when applying an electric field. One of ordinary skill in the art would have been motivated to do this because the Weidlich invention involves delivery of a drug (anti-inflammatory steroid), offering a device which accomplishes in a single step the methods of Zewert et al. and procedures performed in Widera et al. Moreover, Widera et al. concludes that "in vivo electroporation substantially increases DNA delivery and

DNA vaccine potency, appears to be well tolerated by the animals, and is a simple technique that takes only a few seconds after inoculation" (page 4640, second paragraph). A holding of obviousness is clearly required.

Applicant's arguments filed August 19, 2005, have been fully considered but they are not persuasive. With respect to the Zewert reference, the Applicant asserts that the non-penetrating electrodes of Zewert et al. do not cause the nucleotide component to be delivered into the cells of the organism. However, Zewert et al. indicates that the invention can be used for electroporating tissue, "whereby at least a portion of the composition **enters** or passes across the tissue, thereby delivering the nucleotide into the tissue" (column 4, lines 52-55, emphasis added). Thus, nucleotides are delivered into tissue cells. Moreover, claim 1 recites that the stratum corneum is electroporated, and "at least a portion of the composition **enters** or passes across the stratum corneum, thereby delivering the nucleotide component into the organism" (emphasis added). In this case, nucleotides are delivered into the dead cells of the stratum corneum.

Further still, Applicant notes that the electrodes employed in Zewert et al. do not penetrate into tissues, and thus do not meet the limitations of the claimed invention of an electrode which penetrates into tissues and delivers molecules into biological cells in the penetrated tissues. It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. There is nothing in Zewert et al. that prevents the electrodes used in practicing the Zewert invention from being inserted into the skin, through the stratum corneum. Moreover, Zewert et al. is combined in an

obviousness rejection with Weidlich et al., which teaches an electrode with a coating which in inserted into tissue.

With respect to the Widera reference, the Applicant argues that Widera et al. requires three apparatuses in contrast to the two required by the instant application, wherein a coated electrode is used. However, it is respectfully pointed out that Widera et al. is used in combination with Weidlich et al. which teaches a coated electrode.

Claims 25, 26, 28, 29, 30, 31, 37, 44, 47, 49, 50, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weidlich et al. and Hofmann as applied to claims 25, 26, 28, 29, 30, 31, 37, 49, 50, and 52 above, and further in view of Lerner (WO 97/18855).

As discussed above, Weidlich et al. and Hofmann render claims 25, 26, 28, 29, 30, 31, 37, 49, 50, and 52 obvious. However, these references do not expressly disclose protein-based vaccines in the polymeric coating of the implantable, stimulating electrode taught by Weidlich et al.

Lerner discloses a drug delivery device comprising electrodes supporting a "drug or other biologically active substance or compound" (claim 9). Furthermore, drugs or other biologically active substances for delivery include bacterial vaccines (page 28, line 7), proteins (page 28, line 19), and viral vaccines (page 28, line 22).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have included protein-based vaccines in the polymeric coating of the Weidlich electrode to be delivered when applying an electric field. One of ordinary skill in the art would have been motivated to do this because Lerner teaches that a variety of drugs can be delivered

when using electrodes. It would have been desirable to deliver protein-based drugs for vaccination of bacterial and viral diseases. Moreover, since the Weidlich electrode is suitable for delivering a drug (anti-inflammatory steroid), one of ordinary skill in the art would have recognized the suitability of delivering other drugs in the same manner by including the drug in a coating on the electrode. A holding of obviousness is clearly required.

Applicant's arguments filed August 19, 2005, have been fully considered but they are not persuasive. Applicant asserts that Lerner does not teach the delivery of material into cells using electroporation. However, delivery of material occurs when practicing the Lerner invention, since in one embodiment, the active compound delivered passes the blood brain barrier (page33, lines 10-12). Clearly the active compound have to have been delivered into and out of cells of the blood brain barrier.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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